About 4,000 patients will continue to be followed as part of the Early Treatment Diabetic Retinopathy Study to answer the study's two remaining questions:

1. When in the course of diabetic retinopathy is it most effective to initiate photocoagulation therapy?

2. Is aspirin effective in altering the course of diabetic retinopathy?

JAMES L. KINYOUN, MD
Seattle

REFERENCES

Klein R, Klein BEK, Moss SE, et al: The Wisconsin epidemiologic study of diabetic retinopathy—IV. Diabetic macular edema. Ophthalmology 1984 Dec; 91:1464-1474

The Diabetic Retinopathy Study Research Group: Preliminary report on effects of photocoagulation therapy. Am J Ophthalmol 1976 Apr; 81:383-396

The Early Treatment Diabetic Retinopathy Research Group: Photocoagulation treatment of diabetic macular edema. Arch Ophthalmol 1985 Dec; 103:1796-1806

The Early Treatment Diabetic Retinopathy Study Manual of Operations. ETDRS Coordinating Center, Maryland Medical Research Center, 600 Wyndhurst Avenue, Baltimore, MD 21210 (rev 5/1/85)

Treatment of Macular Pucker

THE TERM MACULAR PUCKER refers to membranes overlying or distorting the macula or foveal region of the retina, causing a significant reduction in central vision. These membranes may occur spontaneously; they are also a major cause of poor central vision following surgical correction of a retinal detachment due to a retinal hole. Epiretinal membranes are often seen in diabetic retinal disease.

Puckering of the macula occurs when contraction of the preretinal membranes causes wrinkling of the underlying retina. This is accompanied by distortion and reduction in visual acuity. These preretinal membranes may very rarely separate from the retina spontaneously, with improvement in vision.

Vitreous surgical techniques can be used to remove epiretinal membranes. The success rate of this operation is high, with visual improvement occurring in up to 90% of cases. The greatest amount of improvement occurs in cases with the greatest degree of visual reduction. Vision limited to counting fingers may be improved to the 20/100 level even after several years of reduced vision. Visual distortion may also improve significantly following surgical repair.

Complications are uncommon but do occur. They include retinal detachment, recurrence of the epiretinal membranes on rare occasions and cataract.

MAURICE B. LANDERS, MD
Sacramento, California

REFERENCES

Michels RG: Vitreous surgery for macular pucker. Am J Ophthalmol 1981 Nov; 92:628-639

Michels RG, Gilbert HD: Surgical management of macular pucker after retinal reattachment surgery. Am J Ophthalmol 1979 Nov; 88:925-929

Shea M: The surgical management of macular pucker in rhegmatogenous retinal detachment. Ophthalmology (Rochester) 1980 Jan; 87:70-74

Botulinum Toxin Therapy in the Management of Strabismus and Lid Disorders

IN 1973 Scott, Rosenbaum and Collins reported on the use of various drugs injected directly into the extraocular muscles of monkeys. The drugs used were diiosopropyl fluorophosphate, cobra neurotoxin, botulinum neurotoxin and alcohol. The goal was to discover a pharmacologic means of producing a long-term paralysis of the injected muscle while causing minimal systemic involvement. Botulinum toxin appeared to satisfy these requirements.

In 1981 Scott reported on the results of 132 injections in 42 humans. In 1982 he initiated a prospective multicenter clinical trial to evaluate the safety and efficacy of botulinum toxin under a Food and Drug Administration protocol. To date, more than 5,000 patients have been injected, and the study is still under way.

Six antigenically different types of botulinum toxin have been identified. Type A neurotoxin is the only one used pharmacologically at this time; it is a single polypeptide chain with a molecular weight of about 150,000.

Botulinum toxin appears to act by interfering with acetylcholine release from the nerve terminal. It acts on individual muscle terminals presynaptically, but apparently does not affect the electrical excitability or conduction in either the muscle or nerve. The doses used seem to be below the threshold of recognition by the immune system, thus allowing repeated injections.

The therapeutic principle of botulinum toxin in strabismus is to paralyze the injected muscle. The paralysis usually lasts four to eight weeks, during which time the antagonist muscle has a chance to contract or gain strength. When the pharmacologic effect wears off, the forces should then be balanced. In other words, the injected muscle will have undergone a weakening procedure or chemical "recession" and the antagonist muscle will have undergone contracture or a "resection." Botulinum toxin can also be used to prevent contracture of a muscle when the antagonist muscle is paralyzed and when one is awaiting recovery of that paralysis, such as in a case of acute sixth nerve palsy.

Adults are injected using only topical anesthesia. A special portable electromyographic recorder is attached to a monopolar or bipolar electrode in a uniquely designed hypodermic needle. In the tip of the hypodermic needle is the electrode used for proper placement of the neurotoxin in the muscle. The needle is inserted subconjunctivally and is then passed into the desired muscle, with that muscle undergoing contracture. Usually 0.1 ml of toxin is injected. The dosages range between 1×10^{-3} and 1×10^{-2} μg, or 1/200th the median lethal dose level for humans.

Considerable clinical experience has occurred during the past several years. The absolute indications are not yet completely clear, however, although several principles seem to be emerging. There is much more widespread usage of the drug in adults than in children because of the need to use ketamine hydrochloride anesthesia for children and the need for reinjection, at least at current protocol dose schedules. There is more enthusiasm for injecting the horizontal rectus muscles than the vertical rectus muscles, as they are easier to inject. Also, in superior rectus injections there is involvement of the lid, and in the inferior rectus injections, the inferior oblique muscle is involved. The mean correction per injection is about 20 prism diopters. Thus, the ideal patient appears to be one with horizontal strabismus of small to moderate size.

There are several strabismic conditions for which botulinum toxin injection is ideal. These include chronic sixth nerve palsy when accompanied by a transposition procedure, acute sixth nerve palsy to prevent secondary contracture and acute thyroid ophthalmopathy when surgical treatment is not yet indicated. Phthisis, active inflammation or severe glau-

coma may be exacerbated by an operation. These all can be treated with botulinum toxin. Small-angle strabismus, especially surgical undercorrections and overcorrections when one does not desire to reoperate, are also good indications.

Side effects have been minimal, but include globe perforation from the injection needle, transient ptosis and temporary adjacent muscle paresis with induced vertical deviation. No serious systemic side effects have been reported.

The drug has also been useful for the temporary but dramatic relief of benign essential blepharospasm and hemifacial spasm. For these disorders, the paralysis of the orbicularis may last several months. Spastic entropion has also been relieved temporarily by botulinum injection.

ARTHUR L. ROSENBAUM, MD
Los Angeles
ALAN B. SCOTT, MD
San Francisco

REFERENCES

Perman KI, Baylis HI, Rosenbaum AL, et al: The use of botulinum toxin in the medical management of benign essential blepharospasm. Ophthalmology, in press

Scott AB: Botulinum toxin injection of eye muscles to correct strabismus. Trans Am Ophthalmol Soc 1981; 79:734-770

ADVISORY PANEL TO THE SECTION ON OPHTHALMOLOGY